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ON
PUBLIC HEALTH AND MEDICAL SUBJECTS

No. 33.

A REPORT ON
THE NATURAL DURATION OF CANCER

By

MAJOR GREENWOOD, F.R.C.P.

MINISTRY OF HEALTH.

LONDON:
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PREFATORY NOTE BY THE CHIEF MEDICAL OFFICER.

To The Right Hon. NEVILLE CHAMBERLAIN, M.P.,
Minister of Health.

SIR,

At an early stage in its consideration of the questions confronting it the Departmental Committee on Cancer* realized the potential value of a standard of comparison by means of which the success of various methods of treatment can be judged, and the object of the following report by Dr. Major Greenwood, one of the Medical Officers of the Ministry, is to provide a standard of this nature. The author points out that precise measurement is impossible. The data which he has analysed, although superior to any hitherto published, are subject to unavoidable errors and certain statistical difficulties of interpretation. In the treatment of cancer, as in other diseases, the individuality of each patient and the special circumstances of each case, from the clinical and pathological points of view, are such important elements of prognosis that statistical averages have little practical value *in the individual case*. The method described does, however, enable the *average* results of one kind of treatment to be compared with those of another kind.

On the other hand, when the subject is examined from the communal aspect statistical results are extremely valuable. I may draw attention to the remarks made in this report upon the advantage enjoyed by those who submit to early operation

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* This Committee, which was appointed in 1923 "to consider available information with regard to the causation, prevalence and treatment of cancer and to advise as to the best method of utilising the resources at the disposal of the Ministry for the study and investigation of these problems," consists of the following members:—

Sir George Newman, K.C.B., M.D., F.R.C.P. (Chairman).
C. J. Bond, C.M.G., F.R.C.S. (Hon. Consulting Surgeon, Leicester Royal Infirmary).
Sir George Buchanan, C.B., M.D. (Ministry of Health).
S. Monckton Copeman, M.D., F.R.C.P., F.R.S. (Ministry of Health).
Major Greenwood, F.R.C.P. (Ministry of Health).
Professor Sir F. Gowland Hopkins, D.Sc., M.B., F.R.C.P., F.R.S. (Bio-chemical Department, University of Cambridge).
Professor W. S. Lazarus-Barlow, M.D., F.R.C.P. (late of Cancer Department, Middlesex Hospital).
J. A. Murray, M.D., F.R.S. (Imperial Cancer Research Fund).
T. H. C. Stevenson, C.B.E., M.D. (General Register Office).
S. Wyard, M.D., M.R.C.P. (The Cancer Hospital, Kensington).
Lt.-Col. A. B. Smallman, C.B.E., D.S.O., M.D. (Ministry of Health), (Secretary).

for cancer of the breast. Since Dr. Greenwood prepared this report the Departmental Committee have had the advantage of consulting excellent records of cases of women operated upon for undoubted cancer of the breast in various provincial cities. The results confirm Dr. Greenwood's arresting conjecture that resort to early operation in cancer of the breast would, in the aggregate, add thousands of years to the active life of the nation.

The Ministry is greatly indebted to Sir George Beatson, K.C.B., Mr. Carter Braine, Professor W. S. Lazarus-Barlow, Dr. G. Powell White and Dr. S. Wyard, who collected the data on which the report is based, not only for undertaking the compilation but also for permitting the use of the material in this form.

I am, Sir,

Your obedient Servant,

GEORGE NEWMAN.

WHITEHALL,
June, 1926.

A REPORT ON THE NATURAL DURATION OF CANCER

By

MAJOR GREENWOOD, F.R.C.P.

Medical Officer (Medical Statistics) Ministry of Health.

In the course of the investigations of the Departmental Committee on Cancer, difficulties have arisen owing to the fact that in the study of cancer from the clinical side, we have had either no well-defined criterion of the success or failure of a method of treatment, or else a definition which might create in the minds of those interested in the subject, and all men are interested in the subject, a false impression. The reason is that the word " cure " is not a technical word but belongs to the current vocabulary, and that its ordinary associations are with the issue of acute diseases. When used in such a connection, little or no inconvenience results from the absence of any special definition. One is in the presence, let us suppose, of a case of acute appendicitis or of strangulated hernia and the conditions have been relieved by surgical operation. To say that the patients have been " cured " is to say something which needs no technical qualification. Had the operations not been performed, in the one case there would have been a considerable probability, in the other, almost certitude, that the patient would have died within a few days ; after their performance the patients are, so far as their expectations of further life are concerned brought back into the category of the general population of the appropriate sex, age and occupation. But when we are dealing, not with an acute illness, the event of which will be decided in a few hours or days, at most a week or two, it is not easy to interpret the word " cure." Thus, suppose we have a straightforward case of pulmonary consumption. There are unequivocal symptoms, cough, loss of weight, etc., definite physical signs, râles, dulness, etc., and complete biological proof, the discovery of tubercle bacilli in the sputum. Such a patient will not, usually, die within a few days. Life may be prolonged for months or years. What is to be the definition of cure ? One naturally grasps at an objective definition. Suppose the symptoms to be relieved, the physical signs unaltered or retrogressive and the bacilli to disappear from the sputum. Is this a " cure " ? If an examination of the after histories of such patients showed that on the average they lived as long as a random sample of persons of the same age, sex, occupation, etc., nobody could object to the use of the word " cure." This condition is not statistically fulfilled. Messrs. Elderton and Perry* examined the mortality experience of persons discharged

* Drapers' Company Research Memoirs, No. VI. *A Third Study of the Statistics of Pulmonary Tuberculosis.* London, 1910.

(18920.) Wt. 28663—3179/2131. 1250. 7/26. Wy. & S., Ltd. Gp. 50 (9).

"apparently cured" from the Adirondack Sanatorium and showed that while, using a standard table of mortality, 19 deaths should have occurred in the period studied, 59 deaths actually occurred. Bardswell and Thompson* in their study of the after histories of Midhurst patients found that the ratio of actual to expected deaths in the class discharged "much improved" was never less than 7 to 1. It follows that, *on the average*, "cure" in the sense we associate with the usual outcome of a successful operation for strangulated hernia is not the outcome of the most enlightened treatment of pulmonary consumption. Naturally this does not mean that the treatment was useless. In the Adirondack experience† about 75 per cent. of the "apparently cured" were still alive at the end of 15 years (it was computed that 85 per cent. of the general population would have survived as long). According to the experience of Laennec and Louis‡ 100 years ago, the average duration of the disease was only two years. In 1849 of 215 cases admitted to the Brompton Hospital only 6·5 per cent. lived more than four years and 78·1 per cent. died within $2\frac{1}{2}$ years. Of Dr. Pollock's 3,566 patients, half a century ago, however, only 129, 3.6 per cent. were dead within $2\frac{1}{2}$ years.

The inference, I think, is that in assessing the results of treatment when any chronic disease is in question, we should not use the word "cure" absolutely. Repugnant as it is, to more people than Edmund Burke, to reduce the phenomena of human life to arithmetical ratios, I would submit that an arithmetical definition of "cure" is necessary. Such a definition has indeed been accepted in much of the surgical literature respecting cancer. Some surgeons define a "cure" as the survival without signs of local recurrence or metastasis 3 or 5 years after operation. So long as such results are specifically mentioned as "three-years cures" or "five-years cures," no misunderstanding can arise. But it is easy for the defining words to be dropped and such results to be spoken of as "cures" without qualification. I suggest that a numerical measure of cure must take account of three quantities, (1) the average duration of life of a person, of the same age as the patient, not known to be suffering from the disease; (2) the average duration of life of a person suffering from the disease and left untreated; (3) the average duration of life of a person suffering from the disease and treated in the manner the value of which it is desired to test. One plan would be to take the ratio, or percentage ratio, of the difference between (3) and (2) to the difference between (1) and (2). For instance, suppose the normal average duration of life from a given age (what is usually called the Expectation of Life) is 20 years, that the untreated victims of some disease live on the average 3 years while those operated upon live on the

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* Medical Research Committee, *Special Report Series, No.* 33. London, 1919.

† *On Diseases of the Lungs and Pleurae*, by Sir R. Douglas Powell and P. Horton-Smith Hartley. London, 1921, p. 628.

‡ Powell and Hartley, op. cit., p. 625.

average 10 years. We might take as an index $\frac{(10-3)}{(20-3)}=\frac{7}{17}$ or 41 per cent. This fulfils some of our requirements. It will be equal to 0 if the treated patients live on the average just as long as the untreated and it will be negative if they die on the average sooner than the untreated. But it is open to the objection that unless the untreated patients survive no time at all, the index will never be unity or 100 per cent. This is repugnant to common sense, for if the operation brings the patient back into precisely the same position as that of persons not known to be suffering from the disease, it seems reasonable to say that it cures 100 per cent. The relevance of the length of natural duration is rather to the *advantage* of the operation. If persons suffering from a disease live on the average *almost* as long as persons without it, a treatment which puts them into the position of living quite as long may not be worth the trouble. Most people would think submitting to a surgical operation a cheap price to pay for an average extension of life of 10 years; few people would purchase an average extension of 10 days on the same terms.

We avoid certain difficulties by taking as denominator, not the difference between the normal duration of life and the duration of life of the untreated, but the normal duration itself. For instance, it avoids the arithmetical absurdity of an indeterminate value when all the quantities are equal. But it remains open to the objection that unless the duration of untreated cases is zero we cannot have 100 per cent. of cures. We should have, in the imagined case $\frac{(10-3)}{20}=35$ per cent. But, perhaps, the members of this ratio rather than the ratio itself give the most useful information. The facts are that the untreated patient enjoys 15 per cent. of the normal life-time and the treated patient 50 per cent. of the normal life-time, hence the treatment confers an average advantage of 35 per cent. of a normal life-time and this is what we ought to say, avoiding altogether the ambiguous word "cure." If, however, we wish to retain that word we must understand it as practically synonymous with "advantage."

Throughout this discussion it has been assumed that we are in a position to determine the average after-duration of life under different conditions at different ages. This we can do, approximately, for the general population. But, as will subsequently appear, we have not sufficient evidence to prove that in cancer the average duration of life from onset differs greatly at different ages. The consequence is that, since the normal duration of after-life of adults decreases steadily with age, any measure of "cure" or "advantage" which involves the normal expectation of life must give better and better results the older the patient. But an average gain of, say, five years at age 45 is not necessarily a smaller advantage than an average gain of five years at age 65, although it is, of course, a smaller fraction of the normal expectation of life. This objection must be had in mind in

assessing the value of measures of "cure" or "advantage" involving mean durations of life (expectation of life), but does not, I think, deprive them of real interest.

Before, however, anything of the sort can be done in relation to cancer we require measures of the three different quantities already mentioned, one only of which, the average duration of life from any age in the general population, is known at all accurately. The duration of life after treatment, is known, but only to a rough approximation, for certain forms of cancer. For the "natural" duration of life of cancer patients we have rather more information, and the object of this report is to collect it.

It is at once obvious that *really* accurate knowledge of the average length of life from the onset of a cancerous process not radically treated—what for brevity we term the Natural Duration of Cancer—can never be had. It might well puzzle an expert pathologist to define the commencement of a "malignant" change, even if the organs of the body in their finest structure were continuously open to his inspection by magic micro-cinematography. He would have to solve a famous problem—when does a heap of stones become a heap? The only criteria of onset, both physical and subjective, are actually applied not by an expert but by the patient. He or she must fix the onset and fix it by reference to something "wrong." Now there are some forms of cancer, for instance cancer of the stomach, where the earliest indications of disease are almost wholly subjective. There is no question of a "lump," perhaps no question even of pain; merely some deviation from the normal in the functioning of the digestive system, which the most acute self-observer could not distinguish from what happens to all men in the oscillations of physiological life within the bounds of normality.

But there are other forms, cancer of the breast or of the tongue, for instance, where something tangible, a lump, a sore, is given. A growth easy for the patient herself to feel in the breast of one woman might need a very expert finger to recognise in the breast of another. But, broadly, there is a great contrast between cancer of the breast or tongue and cancer of the stomach. For the last mentioned site, it is, at present, impossible to obtain any valuable measure of natural duration. Certainly none which would justify the computation of arithmetical measures of "cure." With cancer of the breast or tongue the case is more favourable; we may fairly hope that our measure of duration, still only rough of course, still probably understated, is of real value. The tongue and breast (leaving out of account such numerically unimportant sites as the larynx and the penis) are at one extreme, the stomach and colon at the other. Intermediate (considering again the numerically important sites) are the cervix uteri, the rectum and the oesophagus. Perhaps in order of ease of self-observation by the patient, the sites range from tongue (with mouth) downwards to breast, cervix uteri, rectum, oesophagus, stomach.

It would seem a sufficiently promising investigation to seek measures of natural duration for, at least, cancers of tongue, breast, cervix uteri, rectum and oesophagus.

The data analysed in this report were obtained by the courtesy of several hospital staffs and include 4,238 cases relating to seven primary sites. The two longest series have already been published by their compilers, to whose observations reference should be made.* The fact that a different method of statistical reduction has been used in this report does not imply any divergence of the conclusions drawn. Upon all important points, the conclusions here reached confirm those of Lazarus-Barlow and Leeming and of Wyard.

* Lazarus-Barlow and Leeming, *Brit. Med. Journ.*, Aug. 16th, 1924. Wyard, *Brit. Med. Journ.*, Jan. 31st, 1925.

Andriezen and Leitch's results, giving a mean duration of 20·88 months for cancer of the cervix uteri are consistent with ours (Andriezen and Leitch, *Arch. Middlesex Hosp. Rep. Cancer Res. Lab.* 1906, V. 161).

TABLE I
Whole Series

Recorders.	Number Observed.	Mean Age at Onset (Years).	Mean Duration (Months).	Probable error of mean.	Standard Deviation.	Probable error of difference from Lazarus-Barlow.
BREAST :						
Professor Lazarus-Barlow (London)	243	55·8	39·8	± 1·59	36·83	
Sir George Beatson (Glasgow)	61	56·9	36·5	± 4·11	47·53	− 3·3 ± 4·41
Dr. Wyard (London)	273	53·8	39·6	± 2·04	49·85	− ·2 ± 2·59
Dr. Powell White (Manchester)	59	59·6	32·1	± 2·95	33·54	− 7·7 ± 3·35
Mr. Carter-Braine (London)	15	54·5	30·2	± 3·37	19·39	− 9·6 ± 3·73
Whole Series	651		38·3	± 1·15	43·33	
UTERUS :						
Professor Lazarus-Barlow	914	47·7	22·7	± ·37	16·80	
Sir George Beatson	134	46·6	18·2	± 1·24	21·27	− 4·5 ± 1·29
Dr. Wyard	554	50·0	18·8	± ·46	16·13	− 3·9 ± ·59
Dr. Powell White	147	50·1	20·6	± ·96	17·28	− 2·1 ± 1·03
Whole Series	1,749		20·9	± ·28	17·13	
RECTUM :						
Professor Lazarus-Barlow (Males and Females)	346	55·3	24·3	± ·63	17·30	
” ” ” (Males)	173	55·8	21·4	± ·77	15·00	
” ” ” (Females)	173	54·7	27·1	± ·97	18·90	
Sir George Beatson (Females)	14	54·1	25·7	± 2·97	16·46	
Dr. Wyard (Males and Females)	450	54·5	28·7	± ·99	31·21	+ 4·4 ± 1·17
Dr. Powell White (Males and Females)	77	54·4	25·9	± 1·37	17·82	+ 1·6 ± 1·51
Whole Series	887		26·7	± ·58	25·41	

Recorders.	Number Observed.	Mean Age at Onset (Years).	Mean Duration (Months).	Probable error of mean.	Standard Deviation.	Probable error of difference from Lazarus-Barlow.
TONGUE AND MOUTH (Males) :						
Professor Lazarus-Barlow	225	54·9	16·5	± ·54	12·04	
Sir George Beatson	65	58·5	16·9	± 1·34	16·04	+ ·4 ± 1·45
Dr. Powell White	79	55·6	16·2	± 1·07	14·19	− ·3 ± 1·20
Whole Series	369		16·5	± ·46	13·21	
OESOPHAGUS (Males and Females) :						
Professor Lazarus-Barlow	74	52·0	14·3	± ·90	11·53	
Dr. Wyard	209	55·7	11·4	± ·50	10·69	− 2·9 ± 1·03
Dr. Powell White	16	54·5	9·4	± 1·11	6·60	− 4·9 ± 1·43
Whole Series	299		12·0	± ·42	10·76	
LARYNX (Males and Females) :						
Professor Lazarus-Barlow	57	50·5	14·8	± ·78	8·71	
Dr. Wyard	53	53·2	14·1	± ·99	10·65	− ·7 ± 1·26
Dr. Powell White	19	51·8	15·0	± 2·99	19·30	+ ·2 ± 3·09
Whole Series	129		14·5	± ·67	11·25	
STOMACH (Males and Females) :						
Professor Lazarus-Barlow	118	53·0	17·1	± ·72	11·52	
Dr. Powell White	36	50·7	15·8	± 1·79	15·95	− 1·3 ± 1·93
Whole Series	154		16·8	± ·68	12·58	

In Table 1 are shown the ordinary arithmetic means of the durations and the other elementary facts. As the distributions are extremely asymmetrical, the mean duration being very different from the most frequent, or *modal*, duration (vide infra) the "probable errors" are not at all exact measures of reliability, but the following inferences are justifiable. (1) There is no significant difference between the averages obtained from different sets of data: (2) The age of reputed onset is lower in cancer of the uterus than in disease of other sites: the latter do not differ substantially one from another. (3) The mean duration from reputed onset is greatest for cancer of the breast; there is little difference between cancer of the rectum and cancer of the cervix uteri, perhaps a slight advantage in the former case. For the four remaining sites we have decidedly shorter durations. The material difficulties in the way of comparison have been emphasised above.

In the above Table no attention is paid to age differences; in the following series averages are shown separately for the age groups, Tables 2 (*a*), (*b*), (*c*), and (*d*).

Tables 2 (*a*).

Prof. Lazarus-Barlow's Data.

Breast (Females). (1883–1922)

Age at reputed onset.	No. observed and percentage.		Mean duration (months).	Probable error of mean.*	Standard deviation.
		Per cent.			
25–34	15	6	35·0	± 9·40	53·96
35–44	41	17	33·6	± 3·27	31·10
45–54	61	25	44·8	± 5·31	61·41
55–64	59	24	42·2	± 3·81	43·36
65–74	47	19	44·6	± 3·07	31·13
75 and over ..	20	8	37·2	± 2·59	17·22
Total all ages ..	243	99	39·8	± 1·59	36·83

* These values are only given as rough indications and have been calculated from the ordinary formula:— $\cdot 67449 \times \frac{\sigma}{\sqrt{n}}$ where σ is the empirical standard deviation corrected by the method proposed in Biometrika X, 1914, p. 529. They are minimum measures of variability due to sampling.

Stomach (Males and Females).

Age at reputed onset.	No. observed.	Mean duration (months).	Probable error of mean.*	Standard deviation.
Under 25	1	—	—	—
25–34	5	—	—	—
35–44	23	20·22	± 2·01	14·27
45–54	33	13·55	± 1·07	9·15
55–64	41	16·76	± 1·17	11·14
65–74	15	21·40	± 2·47	14·21
Total all ages ..	118	17·08	± ·72	11·52

Rectum (Females).

Age at reputed onset.	No. observed and percentage.		Mean duration (months).	Probable error of mean.*	Standard deviation.
		Per cent.			
Under 25 ..	1	1	—	—	—
25–34	14	8	33·00	± 5·92	32·86
35–44	18	10	16·33	± 1·41	8·89
45–54	48	28	28·00	± 1·97	20·30
55–64	61	35	27·69	± 1·31	15·19
65–74	23	13	27·00	± 2·05	14·59
75 and up ..	8	5	33·75	± 1·97	8·26
Total all ages ..	173	100	27·14	± ·97	18·90

Rectum (Males).

Age at reputed onset.	No. observed and percentage.		Mean duration (months).	Probable error of mean.*	Standard deviation.
		Per cent.			
Under 25 ..	3	2	—	—	—
25–34	10	6	15·06	± 1·63	7·65
35–44	19	11	25·11	± 2·86	18·53
45–54	39	23	21·62	± 1·38	12·77
55–64	59	34	21·41	± 1·49	16·97
65–74	39	22	21·31	± 1·61	14·89
75 and up ..	4	2	—	—	—
Total all ages ..	173	100	21·42	± ·77	15·00

* See footnote on page 8.

CERVIX. (Females).

Age at reputed onset.	No. observed and percentage.	Per cent.	Mean duration (months).	Probable error of mean.*	Standard deviation.
Under 25	3	—	—	—	—
25–34	94	10	19·09	± ·85	12·14
35–44	295	32	22·00	± ·68	17·29
45–54	316	35	21·95	± ·56	14·73
55–64	150	17	23·68	± ·94	17·00
65–74	49	5	26·02	± 3·15	32·62
75 and up ..	7	1	11·57	± 1·63	6·41
Total all ages ..	914	100	22·72	± ·37	16·80

TONGUE AND MOUTH (Males).

Age at reputed onset.	No. observed and percentage.	Per cent.	Mean duration (months.)	Probable error of mean.*	Standard deviation.
Under 25 ..	1	—	—	—	—
25–34	7	3	9·86	± 1·25	4·93
35–44	33	15	18·09	± 1·11	9·53
45–54	70	31	17·74	± ·96	11·99
55–64	74	33	15·89	± ·98	12·60
65–74	33	15	15·36	± 1.03	8·75
75 and upwards	7	3	15·86	± 3·27	12·83
Total all ages ..	225	100	16·49	± ·54	12·04

TABLES 2 (*b*)

Dr. Wyard's Data.

BREAST (Females).

Age at reputed onset.	No. observed and percentage.	Per cent.	Mean duration (months).	Probable error of mean.*	Standard deviation.
Under 25 ..	1	—	—	—	—
25–34	25	9	33·00	± 5·22	38·74
35–44	45	16	61·00	± 9·44	93·95
45–54	75	28	32·84	± 3·14	40·36
55–64	61	22	32·70	± 2·07	24·06
65–74	56	21	41·04	± 2·72	30·19
75 and upwards	10	4	30·00	± 5·44	25·50
Total all ages ..	273	100	39·57	± 2·04	49·85

* See footnote on page 8.

CERVIX UTERI.

Age at reputed onset.	No. observed and percentage.	Per cent.	Mean duration (months).	Probable error of mean.*	Standard deviation
Under 25 ..	2	—	—	—	—
25–34	42	8	23·43	± 3·64	34·91
35–45	140	25	17·91	± ·71	12·41
45–55	211	38	18·36	± ·66	14·20
55–65	109	20	19·95	± 1·06	16·41
65–75	46	8	16·70	± ·96	9·63
75 and upwards	4	1	—	—	—
Total all ages ..	554	100	18·76	± ·46	16·13

RECTUM (Males and Females).

Age at reputed onset.	No. observed and percentage.	Per cent.	Mean duration months.	Probable error of mean.*	Standard deviation.
15–24	8	2	17·25	± 2·61	10·92
25–34	29	6	47·69	± 10·01	79·94
35–44	56	12	27·32	± 2·41	26·75
45–54	126	28	28·48	± 1·38	22·96
55–64	135	30	28·47	± 1·70	29·24
65–74	84	19	24·79	± 1·34	18·19
75 and upwards	12	3	27·50	± 4·20	21·54
Total all ages ..	450	100	28·65	± ·99	31·21

OESOPHAGUS (Males and Females).

Age at reputed onset.	No. observed.	Mean duration (months).	Probable error of mean.*	Standard deviation
Under 25	1	—	—	—
25–34	2	—	—	—
35–44	23	15·52	± 2·15	16·04
45–54	70	10·54	± 1·91	23·64
55–64	80	9·68	± ·55	7·32
65–74	29	11·28	± 1·70	13·61
75 and upwards ..	4	—	—	—
Total all ages ..	209	11·35	± ·50	10·69

* See footnote on page 8.

LARYNX (Males and Females).

Age at reputed onset.	No. observed.	Mean duration (months).	Probable error of mean.*	Standard deviation
25–34	2	—	—	—
35–44	8	9·75	± 1·29	5·41
45–54	16	16·13	± 2·43	14·38
55–64	25	14·76	± 1·31	9·77
65–74	2	—	—	—
Total all ages ..	53	14·09	± ·99	10·65

TABLES 2 (*c*).

Dr. Powell White's Data.

BREAST (Females).

Age at reputed onset.	No. observed.	Mean duration (months).	Probable error of mean.*	Standard deviation
25–34	1	—	—	—
35–44	9	17·00	± 3·46	15·38
45–54	9	57·00	± 14·30	63·58
55–64	15	28·60	± 3·96	22·75
65–74	14	28·71	± 4·88	27·10
75 and upwards ..	7	40·71	± 10·62	41·69
Total all ages ..	55	32·78	± 3·14	34·54

(*Note.*—Additional data were obtained from Manchester which were included in the results for the whole series (Table 1). The figures were small and it was not considered necessary to recalculate the means for the separate age groups.)

CERVIX UTERI

Age at reputed onset.	No. observed.	Mean duration. (months).	Probable error of mean.*	Standard deviation.
25–34	8	19·50	± 2·71	11·36
35–44	34	19·59	± 1·75	15·16
45–54	54	16·40	± ·86	9·34
55–64	32	21·75	± 1·85	15·47
65–74	7	43·29	± 13·77	54·03
75 and upwards	2	—	± —	—
Total	137	20·12	± ·97	16·89

* See footnote on page 8.

TONGUE AND MOUTH (Males).

Age at reputed onset.	No. observed.	Mean duration (months).	Probable error of mean.*	Standard deviation.
25–34	1	—	—	—
35–44	12	14·50	± 1·69	8·66
45–54	22	14·45	± ·86	5·98
55–64	24	14·25	± 1·07	7·74
65–74	9	25·00	± 6·53	29·04
75 and upwards	4	—	—	—
Total	72	15·25	± ·95	11·93

RECTUM (Males and Females).

Age at reputed onset.	No. observed.	Mean duration (months).	Probable error of mean.*	Standard deviation.
Under 25	1	—	—	—
25–34	5	—	—	—
35–44	11	13·91	± 2·62	12·91
45–54	16	26·25	± 2·73	16·18
55–64	21	27·00	± 3·29	22·37
65–74	14	27·86	± 3·75	20·76
75 and upwards ..	2	—	—	—
Total all ages ..	70	25·46	± 1·47	18·22

TABLES 2 (*d*).

Sir George Beatson's Data.

BREAST (Females).

Age at reputed onset.	No. observed and percentage.		Mean duration (months).	Probable error of mean.*	Standard deviation.
		Per cent.			
25–34	2	3	—	—	18·05
35–44	10	16	17·40	± 3·85	23·46
45–54	14	23	24·00	± 4·23	65·01
55–64	18	30	50·00	± 10·33	62·43
65–74	13	21	51·46	± 11·68	—
75 and over ..	4	7	—	—	—
All ages ..	61	100	36·54	± 4·11	47·53

* See footnote on page 8.

CERVIX UTERI.

Age at reputed onset.	No. observed and percentage.		Mean duration (months).	Probable error of mean.*	Standard deviation.
		Per cent.			
25–34	9	13	17·67	± 4·63	20·56
35–44	32	47	13·13	± 0·75	6·28
45–54	17	25	12·88	± 0·87	5·34
55–64	9	13	21·00	± 3·61	16·04
65–74	—	—	—	—	—
75 and over ..	1	2	—	—	—
Total all ages ..	68	100	15·35	± 0·92	11·29

TONGUE AND MOUTH (Males).

Age at reputed onset.	No. observed and percentage.		Mean duration (months).	Probable error of mean.*	Standard deviation
		Per cent.			
25–34	1	1·5	—	—	—
35–44	8	12	13·50	± 1·61	6·71
45–54	17	26	16·41	± 3·40	20·73
55–64	18	28	15·67	± 1·54	9·70
65–74	16	25	21·75	± 3·86	22·89
75 and over ..	5	8	—	—	—
Total all ages ..	65	100·5	16·94	± 1·34	16·04

UTERUS AND CERVIX UTERI.

Age at reputed onset.	No. observed and percentage.		Mean duration (months).	Probable error of mean.*	Standard deviation.
		Per cent.			
15–24	1	1	—	—	—
25–34	14	10	28·71	± 9·68	53·69
35–44	51	38	14·41	± 1·17	12·44
45–54	40	30	17·85	± 1·77	16·69
55–64	22	16	18·82	± 1·63	11·32
65–74	4	3	—	—	—
75 and over ..	2	1	—	—	—
All ages ..	134	99	18·22	± 1·24	21·27

* See footnote on page 8.

RECTUM (Females).

Age at reputed onset.	No. observed.		Mean duration (months).	Probable error of mean.*	Standard deviation.
25–34	2				
35–44	—				
45–54	6	14	25·71	± 2·97	16·46
55–64	4				
65–74	1				
75 and over ..	1				

It will be seen that either there is no significant relation between age at onset and duration or, at the least, these data are not numerous enough to establish it. Let us take, as an example, Wyard's series for cervix uteri. In no age group does the mean duration differ by so much as twice its probable error from the average for all ages. Lazarus-Barlow's series confirms the impression. Such apparent exceptions as there are have easy explanations. For example, in the Wyard Series for cancer of the breast, the duration in the age group 35–44 is much longer than at other ages. The size of the standard deviation, however, warns us that something is peculiar. In fact, this group includes two instances of duration above 30 years, another of 15 years and two beyond 9 years. The peak in age group 25–34 of the series for rectum is similarly influenced by abnormal particular cases; a duration of more than 30 years, another beyond 20 years, a third of 9 years. It is possible that, in younger women, duration is more accurately stated and that this affects the comparability, but on the testimony of these data we cannot confirm the general opinion of clinicians that age at onset is an important factor of duration. It should be remarked that the mean duration† is so small in comparison with the average duration of life from *any* age within the range (the average after-lifetime at the age of 70 exceeds 8½ years in both sexes) that the decrease of normal expectation of life with age is unimportant, in comparison with the difference between the expectation of the untreated patient and that of a normal person at any age within the range. We seem at least justified in ignoring age at onset in making a standard of comparison.

So far, we have examined the ordinary arithmetic average-duration. This average, however, puts the case in too favourable a light. One tends to think of the (arithmetic) average as the measure of what usually happens or most frequently happens. In the large number of instances where the character is distributed

* See footnote on page 8.

† As the mean durations for Cancer cases are computed, virtually, from a record of deaths they ought, theoretically, to understate the "true" durations. For reasons explained in Appendix II, the error is probably unimportant.

symmetrically or nearly symmetrically that is really true, the most frequent stature in a population of adults is actually very nearly the arithmetic average of the statures of all adults. But there are many cases when this is not true at all. The most frequent score at cricket is not the arithmetic average of all scores made by cricketers, but a "duck". The most commonly received income is a good deal less than the arithmetic mean of all incomes. Such is the case here; the existence of a small number of persons who survived a very long time has pulled up the arithmetic average. No doubt the best average to use would be the most fashionable value, or mode; but, for technical reasons, this is difficult to calculate unless one has a large number of finely grouped data, and almost equally good results are obtained by choosing the median value, *i.e.*, the value midway between the longest and shortest durations. We can supplement it by the quartiles, *i.e.*, the values exceeded respectively by 75 per cent. and 25 per cent. of the observations. These further averages are shown in Table 3 for the most important sites.

TABLE 3.

Median and Quartiles of Distribution.

	25 per cent. (months).	50 per cent. (months).	75 per cent. (months).
Prof. Lazarus-Barlow's data :			
Cervix	12·0	17·0	25·5
Rectum	12·0	21·0	24·0
Breast	17·8	27·5	49·0
Tongue and Mouth ..	8·0	13·0	18·0
Dr. Wyard's data :			
Cervix	10·0	14·0	20·0
Rectum	11·0	21·0	34·0
Breast	13·0	24·0	40·0
Oesophagus	6·0	8·0	12·0

It will be seen that the mean and median are often far apart. While the actual arithmetic average duration of cancer of the breast is over three years, half the patients are dead within a little more than two years and 3 months, 25 per cent. do not live more than 18 months, and only 25 per cent. survive beyond 4 years 1 month. For cancer of the rectum the difference is less striking, the arithmetic mean duration is only three months longer than the median value. For cancer of the tongue, the absolute difference is no more but, relatively to the shorter total duration, it is more important.

One may now pass to consider the significance of the results from the statistical point of view. In the first place, let us examine the rates of mortality and use for that purpose Lazarus-Barlow and Wyard's data for Cancer of the Breast, Cervix Uteri and Rectum.

In Table 4 are shown the numbers of observations, rates of mortality and computed standard errors, the latter based upon the mean probability of dying, *i.e.*, the ratio of all deaths to all exposed to risk.* Judged by this criterion it is evident that the course of mortality in time is not the same in cancer of the breast as in cancer of the cervix uteri; the maximum mortality is significantly later in the former case. At each year of exposure until the seventh the mortality from cancer of the breast is lower than that from cancer of the cervix, but, as the standard errors indicate, the significance of the observed differences decreases as the period of observation increases.

TABLE 4.

Natural Duration.

Survivors after six years. (*Data of Prof. Lazarus-Barlow and Dr. Wyard.*)

Exposed to Risk.		Deaths.	Probability of dying (Death rate).	Survivors.
Breast : Total observed = 516.				
years.				
0	516	82	·159 ± ·020	1,000
1	434	143	·330 ± ·021	841
2	291	104	·357 ± ·026	564
3	187	58	·310 ± ·033	362
4	129	40	·311 ± ·039	250
5	89	25	·281 ± ·047	172
6	64	15	·234 ± ·056	124
Cervix : Total observed = 1,468.				
years.				
0	1,468	397	·270 ± ·013	1,000
1	1,071	682	·637 ± ·015	730
2	389	228	·586 ± ·025	265
3	161	79	·491 ± ·039	110
4	82	36	·439 ± ·055	56
5	46	20	·435 ± ·073	31
6	26	4	·154 ± ·097	18
Rectum (Male and Female): Total observed = 796.				
years.				
0	796	195	·245 ± ·017	1,000
1	601	260	·433 ± ·020	755
2	341	172	·504 ± ·026	428
3	169	78	·462 ± ·037	212
4	90	47	·522 ± ·051	113
5	43	18	·419 ± ·074	54
6	25	9	·360 ± ·097	31

* See Footnote *supra* p. 15. The figures following the signs ± are standard deviations, not "Probable errors."

A very interesting question is whether after reaching a maximum (in the third year in cancer of the breast, in the second year in cancer of the cervix uteri) the rate of mortality declines in such a fashion that it might be expected in a reasonable number of years to approximate to a normal figure. The statistics do not suggest anything of the kind. On their warrant, we should say that after the third year there is little variation, at best a slight downward tendency. The lowest rate in the series, and that subject to an error of some fifty per cent., is far above the normal level. The mean age of onset is well below 60 years and the probability of dying does not reach the figure of 0·154 in the general population of women until after the age of 80. The highest rate of mortality shown, that for cervix uteri in the second year from onset, is greater than the (somewhat conjectural) mortality rate of centenarians. At no observed epoch from onset is the rate of mortality of the same order of magnitude as normal mortality.

It will now be convenient to express our results in a form which, since it merely uses the information already presented, adds nothing to our absolute knowledge but throws it into a more readily assimilable form and helps us to apply the proposed standards of "cure." The rates of the last table are, at least in form, true probabilities of dying. But if the chance one has of dying in the first year measured from some fixed point in time is q_1, and therefore the chance of not dying $1-q_1$; and similarly if the chance that a person who has lived through the first year will live through the second year be $1-q_2$ and so forth, we can make a *Survivorship Table* in the following way. We begin with some arbitrary round number, say 1,000. These 1,000 are our entrants; at the end of 1 year there will be $1{,}000\,(1-q_1)$ left, at the end of two years $1{,}000\,(1-q_1)\,(1-q_2)$ and so forth. The results of such a series of calculations are shown in Table 5.* Of course these figures are subject

TABLE 5.

SURVIVORS.

Natural Duration Series. (*All data.*)

Years.	Exposed to risk.	Deaths.	Death rate.	Survivors.
		Breast.		
0	651	110	·169	1,000
1	541	181	·335	831 ± 14·7
2	360	136	·378	553 ± 19·5
3	224	69	·308	344 ± 18·6
4	155	50	·323	238 ± 16·7
5	105	27	·257	161 ± 14·4
6	78	18	·231	120 ± 12·7

* In the particular circumstances of these data, where all exits are by death, there is no need to make the calculation. The survivorship table is given by the exposed to risk. All we have to do is to divide throughout by the first entry and multiply by 1,000. The above method, is, however, applicable in all cases when rates of mortality are known, e.g. when cases pass out of observation. Hence it is well to think of a survivorship table as constructed in that way.

Years.	Exposed to Risk	Deaths.	Death rate.	Survivors.
		Cervix.		
0	1,749	501	·286	1,000
1	1,248	796	·638	714 ± 10·8
2	452	268	·593	258 ± 10·5
3	184	86	·467	105 ± 7·3
4	98	43	·439	56 ± 5·5
5	55	24	·436	31 ± 4·2
6	31	5	·161	18 ± 3·2
		Rectum (M. & F.).		
0	887	213	·240	1,000
1	674	289	·429	760 ± 14·4
2	385	196	·509	434 ± 16·6
3	189	88	·466	213 ± 13·8
4	101	53	·525	114 ± 10·7
5	48	21	·438	54 ± 7·6
6	27	9	·333	30 ± 5·8
		Tongue and Mouth (M.).		
0	369	162	·439	1,000
1	207	147	·710	561 ± 25·8
2	60	35	·583	163 ± 19·2
3	25	12	·480	68 ± 13·1
4	13	5	·385	35 ± 9·6
5	8	2	·250	22 ± 7·6
6	6	2	·333	16 ± 6·6
		Oesophagus (M. & F.).		
0	299	209	·699	1,000
1	90	62	·689	301 ± 26·5
2	28	15	·536	94 ± 16·9
3	13	8	·615	43 ± 11·8
4	5	2	·400	17 ± 7·4
		Larynx (M. & F.).		
0	129	71	·550	1,000
1	58	40	·690	450 ± 43·8
2	18	13	·722	140 ± 30·5
3	5	3	·600	39 ± 17·0
4	2	—	—	16 ± 10·9
		Stomach (M. & F.).		
0	154	74	·481	1,000
1	80	47	·588	519 ± 40·3
2	33	15	·455	214 ± 33·1
3	18	13	·722	117 ± 25·9
4	5	3	·600	32 ± 14·3

to random error, which must be some function of the rates of mortality (or survival) upon which they depend. In Appendix I, the method actually adopted to obtain some rough measure of this reliability is shown. This measure, which cer-

tainly does not overstate the uncertainty, makes clear, what indeed common sense would tell us, that after the sixth year in the longest series and much sooner in the short series, the surviving cohort is quite unreliable, as a general measure; the data simply do not suffice to provide a basis for rational conjecture.

For the present we will consider only the case of cancer of the breast as an example of how, with the data of natural duration, we may try to measure the effects of treatment.

We will take it that the mean duration of life from reputed onset is 3·25 years; our present data are certainly sufficient to assure us that 3·25 years is not far from the truth. To estimate the mean duration of life after operation involves a much larger element of conjecture. The mere success of the operation ensures that. We have seen that in a few years, even in the Breast series, the numbers exposed to risk have dwindled to less than 12 per cent. of those originally exposed to risk. Even if these included instances of very long life due to a mistake of diagnosis or an error of stated duration, the consequence might not be very serious (see, however, *supra* p. 16). But for operated cases our experience of the rates of mortality later than the fifth year from operation is very small, and later than the tenth year it is, statistically, worthless. So that in preparing a survivorship table or in estimating mean duration of life, we must introduce some assumption. The assumption made in Lane Claypon's report* was that after 10 years the rate of mortality became normal and approximated to that of the general population of women at the age of 65, thereafter following the normal age mortality table. This may be something of an over-statement. On the other hand, as we have seen, the arithmetical mean duration of life in patients not radically treated is really a too optimistic summary of what usually happens to them. Of course the fact of our having over-estimated both members of the comparison for different reasons is not the least guarantee that our final result is right. It is, however, fair to say that in making the comparison the evidence has not been deliberately selected to favour one side.

Upon these assumptions then we have the following summary results. The normal expectation of life of a woman aged 55 is 18·87 years, the expectation of life of a woman with untreated cancer of the breast is 3·25 years, the expectation of life of a woman operated on under "average" conditions is 5·74 years, and of a woman operated on under the best conditions is 12·93 years.† By "average" conditions are to be understood those in which women

* Reports on Public Health and Medical Subjects, No. 28. Ministry of Health. Cancer of the Breast and its Surgical Treatment, 1924.

† These results are not the same as those printed in Lane Claypon's report. Owing to an oversight, for which I am responsible, the expectation of life of operated patients was stated to be the mean duration from operation plus one year (the estimated mean interval from onset to operation). This is incorrect. One should assume that the mortality in the period before operation was the same as among unoperated patients in the first year.

usually present themselves for radical treatment, *i.e.*, in conditions not too far advanced to render operation with a view to eradication hopeless. On the average such patients have admittedly suffered from the disease for a year before operation. By "best" conditions, we shall understand those of a patient whose cancer is strictly localised, does not involve the skin and has not affected either axillary or supraclavicular glands. Under these circumstances Halsted found that 75 per cent. of his patients were alive 3 years after operation. Recent unpublished information from English sources shows that Halsted's experience was not unduly favourable.

We can now return to the ideas discussed on p. 3. We have found (on certain assumptions) that an untreated victim of cancer of the breast has 17·2 per cent., *i.e.*, $3{\cdot}25/18{\cdot}87 \times 100$ per cent. of the normal duration of life to expect, *on the average*: that a woman operated upon under the most favourable conditions has 68·5 per cent. and one operated upon under the present unsatisfactory conditions has 30·4 per cent. of the normal duration. The advantage secured by the woman operated upon under the most favourable existing conditions is therefore 51·3 per cent. and by the woman under "average" conditions 13·2 per cent. There is much temptation to substitute for this the statement that the operation under the "best" conditions *cures* more than half and under average conditions more than 13 per cent. of the patients, but for the reasons given above I do not think this is fair. Our numerical values are arithmetic means (or approximations to such). If the mean earnings in a certain trade were 40s. a week, and if a person with a certain disability amenable to treatment earned on the average 20s. a week and after treatment earned on the average 30s. a week, we should say that the treatment benefited him to the extent of 25 per cent. of the average normal wage, we should not say that 25 per cent. of those treated earned 40s.; the conclusion does not follow from the premises. Still even the averages do give us a more definite impression of national loss and gain. At the present time the annual quota of new cases of cancer of the breast in England and Wales is probably at least 5,000. Certainly not more than half the patients undergo the radical operation and of these fewer than half again are operated on under the most favourable conditions. Consultation with expert colleagues has satisfied me that this is by no means a pessimistic statement. How many years of life will these 5,000 women, on the average, enjoy? 2,500 of them will have 3·25 years apiece. 1,250 will have 5·74 apiece, 1,250 12·93 years each. The grand total is 31,462·5 years. Had each enjoyed the normal expectation, the total would have been 5,000 multiplied by 18.87 or 94,350 years. If all had been operated on under the most favourable conditions, the quota of years would have been 64,650, more than 30,000 years of life beyond what they will actually have to look forward to. If we make the much more modest assumption, viz., that only the

assumed quarter will be operated upon under the most favourable conditions and the remainder under merely average conditions, we should still secure a bonus of more than 6,000 years of life.

That is the position from the general standpoint. From that of the individual, it may be said that very few normally constituted persons would hesitate to purchase $2\frac{1}{2}$ years and none would hesitate to purchase almost 10 years of life at the price of an operation. It is of course true that no surgeon or medical practitioner can promise 10 years, $2\frac{1}{2}$ years or 3 months. He can do no more than say that these are *averages*. When a considerable element of the subsequent mortality is the immediate effect of the operation, the value of averages in reaching an individual judgment, is of course, much reduced. In the special case of breast cancer, the direct mortality of the most radical operation is now so small that, in my submission, the teaching of the averages is of value even to the individual.

I do not wish to press this illustration. Naturally others may not agree that the proposed arithmetical measures are satisfactory. But it is, I think, certain that whatever measure be adopted, the averages for natural duration must be involved. The information in this report evidently needs extension. It is much to be hoped that similar figures will be compiled in other countries. Apart from the important practical end that, in my submission, they could serve, a comparison of natural durations for different countries might, as Dr. Lane Claypon has pointed out to me, be a proper test for the suggestion that in some races cancer is "naturally" more malignant than in others.

In conclusion I have to thank my colleagues, Miss Woods and Miss Titterton, for making and checking the various calculations.

APPENDIX I.

The "Errors of Sampling" of the Survivorship Tables.

In the preceding pages various tables are given purporting to show how many of an arbitrary number, 1,000, of persons coming under observation will still be alive at the end of 1, 2, 3, etc., years from the moment when the entrants first came under observation. In fact, of course, the numbers of people really observed varied from series to series, there were as many as 1,749 in the series available for computing the survivorship table respecting cancer of the cervix uteri, only 129 for the study of cancer of the larynx. Obviously the result in the former case is more reliable (or less unreliable) than in the latter and one strives to measure the reliability with the help of calculations of "Errors of Sampling." In some cases it is possible to provide very accurate measures of these fluctuations, in others—the present case is an instance—we can only reach approximate values which usually, not always, under-estimate the variability of the results. Why this is so can be understood without any mathematical knowledge. There are two distinct cases of sampling readily illustrated by the familiar schema of a bag of black and white balls. In the first place we make drawings from a bag the composition of which is known, we know, let us say, that half the balls are black and half white. Then the probability that we shall get such or such a deviation from the "expected" proportion of fifty per cent. white and fifty per cent. black in a sample of, say, 100 balls taken out at random is a matter of calculation involving no elements of conjecture, other than that the drawing was really random. But a second and much more frequent case is that we have drawn (at random) 100 balls and found 50 white and 50 black and do not know (except to the extent this sample tells us) what the proportion in the bag is. To do our sum we *must* make some assumption as to the constitution of the bag and actually we always assume that the observed sample is a fair measure of the bag, only making small modifications of our formulae, which, in most cases only alter the results in a rather trivial fashion. For a justification of these processes—so far as they can be justified—reference must be made to text-books of probability and statistics. All I desire to stress here is that the calculations shortly to be described belong wholly to the second class. Our very complicated "bag" contains the whole experience of all persons who have died of cancer untreated; the only knowledge of its contents we possess is afforded by the samples whose reliability we desire to measure.

One other preliminary remark is necessary. For the special case of data of "natural" duration like those considered in this report where every case has been followed from presumed onset to death, an *approximate* measure of statistical reliability can be obtained in a few lines. But when we have—as will be the case in later reports—data not confined to complete observations, the approximation is less easy. I have therefore thought it convenient to deal with the more general case of which the present is a particular example. The algebra offers no novelty, the only, relatively, unusual feature is that we are concerned with a product of terms not a single term.

If the value obtained, from a particular sample, of the probability that a person will survive from time t to time $t+1$ be p_t, from time $t+1$ to time $t+2$ be p_{t+1}, etc., and the value given by the same sample for the probability that he will survive from t to $t+s$, which we will call P, is:—

$$P = p_t \times p_{t+1} \times p_{t+2} \times \cdots\cdots p_{t+s-1} \qquad (1)$$

We require the mean value for all samples or *mathematical expectation* of (1) and the mathematical expectation of the squared deviation of P from its mathematical expectation, i.e., we require E (P) and E $[P-E(P)]^2$. We will suppose that the p's are independent one of another, that an error in p_r,

say, does not make it more, or less, likely that there will be an error in p_s, say. If that be so, and if Δp be some error of a p, we have :—

$$\mathrm{E}\,(\mathrm{P}) = \mathrm{E}\,(p_t) \times \mathrm{E}\,(p_{t+1}) \ldots\ldots \mathrm{E}\,(p_{t+s-1}) \qquad (2)$$

$$\mathrm{P}^2 = p^2_t \times p^2_{t+1} \cdots p^2_{t+s-1}$$

$$\therefore \mathrm{E}\,(\mathrm{P}^2) = \mathrm{E}\,(p^2_t)\,\mathrm{E}\,(p^2_{t+1}) \ldots \mathrm{E}\,(p^2_{t+s-1})$$

$$\therefore \mathrm{E}\,[\mathrm{P} - \mathrm{E}\,(\mathrm{P})]^2 = \mathrm{E}\,(\mathrm{P})^2 - [\mathrm{E}\,(\mathrm{P})]^2$$

$$= \mathrm{E}\,(p^2_t)\,\mathrm{E}\,(p^2_{t+1}) \cdots - [\mathrm{E}\,(p_t)\,.\,\mathrm{E}\,(p_{t+1}) \cdots]^2 \qquad (3)$$

Now p_i, say, $= \mathrm{E}\,(p_i) + \Delta p_i$

$$\therefore \mathrm{E}\,(p^2_i) = \mathrm{E}\,[\mathrm{E}\,(p_i) + \Delta p_i]^2$$

$$= [\mathrm{E}\,(p_i)]^2 + \mathrm{E}\,(\Delta p_i)^2 \text{ if } \mathrm{E}\,(\Delta p_i) = 0$$

which is true if the errors are independent.

Write $\mathrm{E}\,(\Delta p)^2 = \sigma^2{}_{p_i}$

substitute in (3) and we have

$$\left[(\mathrm{E}\,p_t)^2 + \sigma^2{}_{p_t}\right]\ \left[(\mathrm{E}\,p_{t+1})^2 + \sigma^2{}_{p_{t+1}}\right]\ \cdots\ \left[(\mathrm{E}\,p_{t+s-1})^2 + \sigma^2{}_{p_{t+s-1}}\right] - \left[\mathrm{E}\,(p_t) \ldots \mathrm{E}\,(p_{t+s-1})\right]^2$$

$$= \left\{\mathrm{E}\,(p_t) \times \mathrm{E}\,(p_{t+1}) \ldots \mathrm{E}\,(p_{t+s-1})\right\}^2$$

$$\left\{\left(1 + \frac{\sigma^2{}_{p_t}}{[\mathrm{E}\,(p)_t\,]^2}\right)\ \left(1 + \frac{\sigma^2{}_{p_{t+1}}}{[\mathrm{E}\,(p_{t+1})]}\right) \ldots \left(1 + \frac{\sigma^2{}_{p_{t+s-1}}}{(\mathrm{E}\,p_{t+s-1})}\right) - 1\right\}$$

$$= \left\{\mathrm{E}\,(\mathrm{P})\right\}^2\ \left\{\left(1 + \frac{\sigma^2{}_{p_t}}{(\mathrm{E}\,p_t)^2}\right)\ \left(1 + \frac{\sigma^2{}_{p_{t+1}}}{(\mathrm{E}\,p_{t+1})^2}\right) \cdots\cdots \left(1 + \frac{\sigma^2{}_{p_{t+s-1}}}{[\mathrm{E}\,(p_{t+s-1})]^2}\right) - 1\right\} \qquad (4)$$

Now $\sigma^2{}_{p_{t+r}}$ is known if $\mathrm{E}\,(p_{t+r})$ is known, and the number of observations, n_{t+r}, to which p_{t+r} is applied, it is $\dfrac{\mathrm{E}\,(p_{t+r})\,\left[1 - \mathrm{E}\,(p_{t+r})\right]}{n_{t+r}}$.

If the n's are fairly large, then since $\mathrm{E}\,p_{t+r}$ (and similar terms) is not greater than unity, all terms having factors of higher order than n^2_{t+r} in the denominators may be neglected, and (4) becomes—

$$\left\{\mathrm{E}\,(\mathrm{P})\right\}^2\ \left\{\frac{\sigma^2{}_{p_t}}{(\mathrm{E}\,p_t)^2} + \frac{\sigma^2{}_{p_{t+1}}}{(\mathrm{E}\,p_{t+1})^2} + \cdots \frac{\sigma^2{}_{p_{t+s-1}}}{(\mathrm{E}\,p_{t+s-1})^2}\right\} \qquad (5)$$

(4) or, for n of order 50 or more, (5), is the complete formal solution of our problem, i.e., it gives us the standard deviation (the square root of (5)) of sampling, *supposing the p's known.* In fact, we have only a sample. We know that, for instance, n_{s-1} were alive at the beginning of the s^{th} interval, and had a chance of dying through that interval, of these d_s actually died, and we must put $p_s = \dfrac{n_{s-1} - d_s}{n_{s-1}}$

That is we replace the mathematical expectation $(\mathrm{E}\,p_s)$ by the empirical result $\dfrac{n_{s-1} - d_s}{n_{s-1}}$. This is clearly only an approximation (*vide supra*).

In the particular case of data such as those of this report, where all cases are observed to death, formula (5)—as can be verified by a few easy transformations—simplifies to :—

$$\mathrm{E}\left\{\mathrm{P}_s - (\mathrm{E}\,\mathrm{P}_s)\right\}^2 = \frac{n_t - n_{s+t}}{n_t^3}$$ where n_t are the number living at t and n_{s+t}, the number still alive after s intervals of time. This, of course, does not happen when the data are reduced by losses other than deaths, i.e., by lives passing out of observation through being lost sight of.

APPENDIX II.

On the Degree to which the Mean Duration is understated by Hospital Records.

The material used in this report was obtained from entries in hospital records of patients, a large majority of whom died within a few months of coming under observation. Hence estimates of mean duration of life (and rates of mortality) derived from these data are, in principle, subject to the notorious objection to identifying *mean age at death* with mean duration of life or *expectation of life ;* when the record of deaths is derived from a population which is growing. It is well known that, in such circumstances, the mean age at death is much lower than the expectation of life. For instance, the expectation of life of females aged 12 in the County of London Life Table (1911–12) was 53·81 years, calculated by the correct method. The mean age at death in the years used was 58·36 years, which, deducting the 12 years the deceased must have attained, leaves 46·36 years or 13·5 per cent. less than the true value. But, as the recorded mortality and presumably the prevalence of most forms of cancer are increasing, it should follow that the estimates of mean duration in this paper are also under-statements. Lazarus-Barlow and Leeming tested the matter by comparing the mean durations for their series, dividing the data into (1) cases admitted before 1903, (2) cases admitted in and after 1903. I have repeated this in detail with the results shown in the following table.

In the majority of instances the mean duration computed from the more recent series is less (although in no case significantly so, having regard to the probable error of sampling) as theory would lead us to expect. But it is to be noted that although cancer of the breast and cancer of the rectum have *both* increased between 1901 and 1921 at an annual rate of some 3 per cent. (actual deaths), the recorded duration has diminished for the former but increased for the latter site.

Lazarus-Barlow's data.
Mean Duration and Difference between early and later period.

	1883–1902 Mean & its P.E. (No. of Obs.)	1903–1912 Mean & its P.E. (No. of Obs.)	Diff. & P.E. of Difference
Breast..	(99) 42·0 ± 2·84	(144) 38·2 ± 1·82	−3·82 ± 3·37
Uterus	(530) 22·6 ± ·46	(384) 21·3 ± ·65	−1·30 ± ·80
Rectum	(141) 23·0 ± ·94	(205) 25·2 ± ·85	+2·23 ± 1·26
Tongue and Mouth ..	(86) 18·0 ± 1·05	(139) 16·5 ± ·67	−1·50 ± 1·25
Oesophagus	(25) 16·0 ± 1·72	(49) 13·4 ± 1·01	−2·55 ± 1·99
Larynx	(17) 17·5 ± 1·43	(40) 16·4 ± ·88	−1·10 ± 1·68
Stomach	(20) 15·0 ± 1·34	(118) 17·1 ± ·68	+2·09 ± 1·50

These experimental results suggested that the absolute magnitude of the methodological error might be insignificant. This suggestion was confirmed by various theoretical considerations. For instance, an artificial table of mortality for cancer of the breast was constructed, on the rather optimistic assumptions that the true expectation of life from onset was 3·41 years and that 12 per cent. lived more than 7 years. I then computed the mean duration to death from the annual deaths occurring in a population increasing annually at the rate of 5 per cent. and found it to be 3·05 years, an understatement of between 10 and 11 per cent. This is certainly a maximum measure of the understatement. Cancer of the breast is not in fact increasing at this rate while, for the sites showing an increase of this order, the true duration of life when the patient is not treated is, on any plausible hypothesis, less than 3·41 years.

For these reasons, I do not think the methodological error, admittedly involved in the process of calculation, is important. It is improbable that the text durations significantly under-state the true facts. It is even possible that errors of over-statement in the cases of long duration over-compensate the theoretical under-statement.

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1926

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